DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Silver Spring, MD 20993

TRANSMITTED BY FACSIMILE

Eric Gervais, Executive Vice President
Duchesnay, Inc.
919 Conestoga Road
Building One, Suite 203
Rosemont, PA 19010

RE: NDA: 021876
DICLEGIS (doxylamine succinate and pyridoxine hydrochloride) delayed-release tablets, for oral use
MA # 350

WARNING LETTER

Dear Mr. Gervais:

The Office of Prescription Drug Promotion (OPDP) of the U.S. Food and Drug Administration (FDA) has reviewed the Kim Kardashian Social Media Post (social media post) (2015-0069-01) [1] for DICLEGIS (doxylamine succinate and pyridoxine hydrochloride) delayed-release tablets, for oral use (DICLEGIS) submitted by Duchesnay, Inc. (Duchesnay) under cover of Form FDA 2253. The social media post was also submitted as a complaint to the OPDP Bad Ad Program. The social media post is false or misleading in that it presents efficacy claims for DICLEGIS, but fails to communicate any risk information associated with its use and it omits material facts. Thus, the social media post misbrands DICLEGIS within the meaning of the Federal Food, Drug, and Cosmetic Act (FD&C Act) and makes its distribution violative. 21 U.S.C. 352(a), (n); 321(n); 331(a). *See* 21 CFR 202.1(e)(5). These violations are concerning from a public health perspective because they suggest that DICLEGIS is safer than has been demonstrated.

Background

Below are the indication and summary of the most serious and most common risks associated with the use of DICLEGIS.[2]

[1] Posted on Kim Kardashian's verified Instagram (https://instagram.com/p/5Vr42NOS0B/), and verified Facebook (https://www.facebook.com/KimKardashian/posts/10155885009200613:0) pages. The Instagram post is also linked from Kim Kardashian's verified Twitter account (https://twitter.com/KimKardashian/status/622937497333596160). All last accessed, August 7, 2015.

[2] This information is for background purposes only and does not necessarily represent the risk information that should be included in the promotional piece cited in this letter.

According to its FDA-approved product labeling (PI) (emphasis in original):

> DICLEGIS is indicated for the treatment of nausea and vomiting of pregnancy in women who do not respond to conservative management.
>
> **Limitations of Use**
>
> DICLEGIS has not been studied in women with hyperemesis gravidarum.

DICLEGIS is contraindicated in women with known hypersensitivity to doxylamine succinate, other ethanolamine derivative antihistamines, pyridoxine hydrochloride or any inactive ingredient in the formulation, as well as in women who are taking monoamine oxidase inhibitors (MAOIs). The PI for DICLEGIS includes Warnings and Precautions regarding activities requiring mental alertness and concomitant medical conditions. In addition, the most common adverse reaction reported with DICLEGIS was somnolence.

Prior Communication

False or misleading promotional materials by Duchesnay are particularly troubling considering OPDP expressed concerns regarding violative promotional activities for DICLEGIS as recently as November 2013. On November 12, 2013, OPDP sent Duchesnay an Untitled Letter regarding a letter announcing the approval of DICLEGIS. The letter cited in the Untitled Letter was false or misleading because, among other concerns, it omitted all risk information and omitted material facts regarding DICLEGIS' important limitation of use. OPDP is concerned that Duchesnay is continuing to promote DICLEGIS in a violative manner.

Omission of Risk Information

Promotional materials are misleading if they fail to reveal facts that are material in light of the representations made by the materials or with respect to consequences that may result from the use of the drug as recommended or suggested by the materials.

The social media post is misleading because it presents various efficacy claims for DICLEGIS, but fails to communicate any risk information. For example, the social media post includes the following claims:

> OMG. Have you heard about this? As you guys know my #morningsickness has been pretty bad. I tried changing things about my lifestyle, like my diet, but nothing helped, so I talked to my doctor. He prescribed me #Diclegis, and I felt a lot better and most importantly, it's been studied and there was no increased risk to the baby. I'm so excited and happy with my results that I'm partnering with Duchesnay USA to raise awareness about treating morning sickness. If you have morning sickness, be safe and sure to ask your doctor about the pill with the pregnant woman on it and find out more www.diclegis.com; www.DiclegisImportantSafetyInfo.com.

The social media post, however, entirely omits **all** risk information. We note the statement, "[F]ind out more www.diclegis.com; www.DiclegisImportantSafetyInfo.com[,]" appears at the end of the social media post; however, this does not mitigate the misleading omission of risk information. By omitting the risks associated with DICLEGIS, the social media post misleadingly fails to provide material information about the consequences that may result from the use of the drug and suggests that it is safer than has been demonstrated.

Omission of Material Fact

In addition, the social media post is misleading because it fails to provide material information regarding DICLEGIS' full approved indication, including important limitations of use. Specifically, it fails to convey that DICLEGIS has not been studied in women with hyperemesis gravidarum. The Indications and Usage section of the PI states the following (emphasis in original):

> **Limitations of Use**
>
> DICLEGIS has not been studied in women with hyperemesis gravidarum.

Conclusion and Requested Action

For the reasons discussed above, the social media post misbrands DICLEGIS within the meaning of the FD&C Act and makes its distribution violative. 21 U.S.C. 352(a), (n); 321(n); 331(a). *See* 21 CFR 202.1(e)(5).

OPDP requests that Duchesnay immediately cease misbranding DICLEGIS and/or cease introducing the misbranded drug into interstate commerce. Please submit a written response to this letter on or before August 21, 2015, stating whether you intend to comply with this request, listing all promotional materials (with the 2253 submission date) for DICLEGIS that contain presentations such as those described above, and explaining your plan for discontinuing use of such materials, or, in the alternative, for ceasing distribution of DICLEGIS. Because the violations described above are serious and repeated, we request, further, that your submission include a comprehensive plan of action to disseminate truthful, non-misleading, and complete corrective messages about the issues discussed in this letter to the audience(s) that received the violative promotional materials. In order to clearly identify the violative promotional piece(s) and/or activity and focus on the corrective message(s), OPDP recommends that corrective piece(s) include a description of the violative promotional piece(s) and/or activity, include a summary of the violative message(s), provide information to correct each of the violative message(s), and be free of promotional claims and presentations. To the extent possible, corrective messaging should be distributed using the same media, and generally for the same duration of time and with the same frequency that the violative promotional material was disseminated.

Please direct your response to the undersigned at the **Food and Drug Administration, Center for Drug Evaluation and Research, Office of Prescription Drug Promotion, 5901-B Ammendale Road, Beltsville, Maryland 20705-1266** or by facsimile at (301) 847-8444. To ensure timely delivery of your submissions, please use the full address above and include a prominent directional notation (e.g. a sticker) to indicate that the submission is

intended for OPDP. Please refer to MA # 350 in addition to the NDA number in all future correspondence relating to this particular matter. All correspondence should include a subject line that clearly identifies the submission as a Response to Warning Letter. OPDP reminds you that only written communications are considered official.

The violations discussed in this letter do not necessarily constitute an exhaustive list. It is your responsibility to ensure that your distribution of DICLEGIS complies with each applicable requirement of the FD&C Act and FDA implementing regulations.

Failure to correct the violations discussed above may result in FDA regulatory action, including seizure or injunction, without further notice.

Sincerely,

{See appended electronic signature page}

Robert Dean, MBA, RAC
Division Director
Office of Prescription Drug Promotion

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

ROBERT T DEAN
08/07/2015